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Poly(vinyl alcohol)-based Amphiphilic Copolymer Aggregates as Drug Carrying Nanoparticles

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A series of amphiphilic polyisobutylene-block-poly(vinyl alcohol) (PIB-*b*-PVA) copolymers of constant PIB and varying PVA block length was synthesized by living carbocationic polymerization and their solution behavior was studied. The synthesis involved the preparation of polyisobutylene-*b*-poly(*tert.*-butyl vinyl ether) followed by hydrolysis with hydrogen bromide. The copolymers were characterized by gel permeation chromatography, ^{1}H-NMR, and MALDI-TOF MS methods. The micellization behavior of the copolymers was investigated in aqueous media by direct dissolution and dialysis using static and dynamic light scattering. The critical micelle concentration, micelle size, aggregation number, and micelle shape were determined. The ability of the aggregates as drug carrying nanodevices was also investigated by doping them with indomethacin. UV-Vis measurements showed that the solubility of indomethacine increased significantly. Our findings suggest that the solubility is largely dependent upon the block segment ratios.

Keywords: Polyisobutylene, poly(vinyl alcohol), block copolymer, self assembly, indomethacin

1 Introduction

The solubilization of water insoluble drugs has been the focus of surfactant chemistry from the very beginning of the field (1–4). Micellar aggregates formed in aqueous media, such as core-shell micelles, vesicles, cylinders and bilayers, are considered to enhance the solubility of apolar compounds in water through the incorporation of the target molecule to the apolar core or layer of the aggregate (5–9). The building blocks of these aggregates are amphiphilic block copolymers, i.e., block-copolymers consisting of hydrophilic and hydrophobic chains, which have attracted great consideration from both academic and practical points of view (10, 11). When dissolved in water (preferred for the hydrophilic block) or in organic solvents (preferred for the hydrophobic block) amphiphilic block copolymers self assemble into micellar aggregates (12, 13). Typically, the ratio of the two blocks determines the structure of the aggregates (14). When they are of comparable size, the formation of core-shell type micelles is expected, but when the size of the polar block is multiple times that of the apolar block, vesicle formation is most likely. Block copolymers with controlled block length can be prepared by living polymerization (15–18). Our lab has gained expertise in the preparation of polyisobutylene (PIB) based amphiphiles (19–21); therefore, PIB was chosen to be the apolar part of the polymer. For the hydrophylic part, poly(vinyl alcohol) (PVA) was chosen since it is a common polymer used as an additive in pharmaceutics and because of its higly polar nature (21, 22). PVA can be obtained by the hydrolysis of poly(vinyl acetate) or poly(vinyl ethers) such as poly(*tert.*-butyl-vinyl ether) P*t*BVE. Our aim was the synthesis of PIB-PVA diblock copolymers having a constant PIB block length but varying the size of the PVA block. Although Faust et al. reported the synthesis of PVA-PIB-PVA triblock copolymer (23, 24), its micellar properties were not investigated and to the best of our knowledge, diblocks of these two polymers have yet to be synthesized.

In this paper we report on the synthesis, self-assembly and micellar properties of polyisobutylene-*block*-poly(vinyl alcohol) (PIB-*b*-PVA) polymers of different compositions. In addition, the aggregates formed in aqueous media were tested as possible drug carrying nanoparticles.

2 Experimental

2.1 Materials

Titanium (IV) chloride ($TiCl_4$) (99.9%, Aldrich), 2, 6-di-tert-butylpyridine (DTBP) (97%, Aldrich), Titanium

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(IV) isopropoxide ($Ti(OiPr)_4$) (99.999%, Aldrich), methallyltrimethyl silane (97%, Aldrich), and indomethacine (Aldrich) were used as received. *Tert.*-butyl vinyl ether (*t*BVE) was distilled over CaH_2 and was stored at −18°C until use. Hexanes was purified by refluxing over cc. H_2SO_4 overnight then washed with saturated $NaHCO_3$ and distilled water. It was dried over KOH and was distilled over P_2O_5 after a 48 h reflux right before use. CH_3Cl and isobutylene (IB) were dried by passing it through a column filled with $CaCl_2$ and condensed at -80°C prior to polymerization. The synthesis of 2-chloro-2,4,4-trimethylpentane (TMPCl) and ditolylethylene (DTE) have been previously described in the literature (25). Silver trifluoroacetate (AgTFA) (Aldrich, Germany) and 1,8-Dihidroxy-9(10*H*)-anthracenone (dithranol) were used without further purification.

2.1.1. *Preparation of polyisobutylene-block-poly(tert-butyl-vinylether) (PIB-b-PtBVE)*

The polymerizations were carried out in a dry-box under dry nitrogen at −80°C. Hexanes (53.8 mL), MeCl (37.9 mL), DTBP (4.45 mL), TMPCl, and $TiCl_4$ were sequentially added into a 500 mL round bottom flask. This was followed by the addition of IB into the flask after 5 minutes. After polymerization for 1 h, DTE was added and after 1 h, $Ti(OiPr)_4$ was added. The majority of the polymerization mixture was poured into special 75 mL test tubes and the remaining mixture was quenched with pre-chilled methanol. A calculated amount of pre-chilled *t*BVE was added to the mixture in the test tube based on the desired P*t*BVE chain length and polymerized for 1 h. At the end, methallyltrimethylsilane was added and after 30 min, all polymerizations were quenched with pre-chilled methanol. The reaction mixtures were poured into excess 10% ammonical methanol and dried under the hood. The polymers were purified by dissolution in hexanes and precipitation in methanol. The samples were dried in vacuum for 24 h. The polymers were further purified by dissolution in dichloromethane and precipitation with methanol in order to remove hexanes, which can be trapped by the PIB block. This was followed by drying in vacuum for 24 h. The weight of the dry samples was measured and conversion was calculated, which was nearly 100% in each case.

2.1.2. *Preparation of polyisobutylene-block-poly(vinyl-alcohol) (PIB-b-PVA)*

PIB-*b*-P*t*BVE was hydrolyzed to PIB-*b*-PVA with hydrogen bromide (HBr) gas at 0°C. Dry nitrogen was passed through a stirred 1 wt % solution of PIB-*b*-P*t*BVE in anhydrous CH_2Cl_2 to remove oxygen. Then, dry HBr gas was slowly bubbled through for 30 min at 0°C. The mixture was poured into a large amount of ammonical methanol and was allowed to air dry. The polymers were purified by dialysis in distilled water to remove the NH_4Br from the samples. The concentrated samples were dried by freeze drying. The dry polymers formed white foamy solids.

2.2 Solution Preparation

A solution series was prepared from the corresponding PIB-*b*-PVA copolymer sample by direct dissolution in water. Another series was prepared from the corresponding

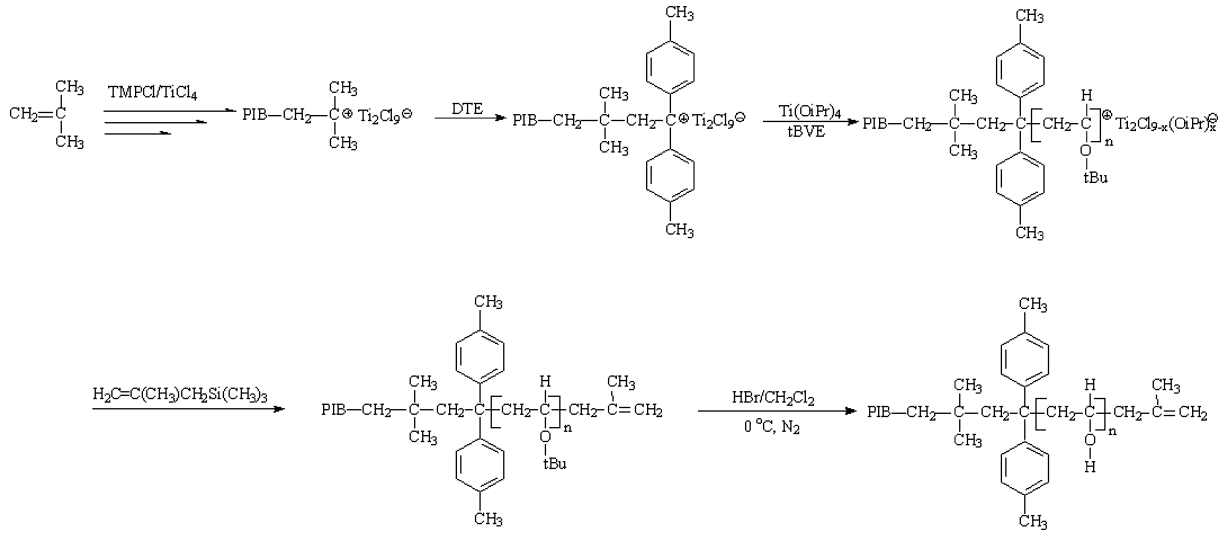
PIB-*b*-PVA copolymer by direct dissolution in N, N-dimethylacetamide followed by dialysis in water for one week. The applied concentration range was from 0.005 to 0.5 mg/mL for all PIB-*b*-PVA samples. The samples were filtered through 1 μm syringe filter and were allowed to equilibrate for 24 h and were measured thereafter.

2.3 Solubilization of Indomethacin

The corresponding PIB-*b*-PVA and indomethacine were dissolved in N, N-dimethylacetamide, mixed well, and dialyzed in water for one week. The dissolved indomethacin quantity was equal to that of the corresponding PIB-*b*-PVA. The solubility of indomethacin is lower in water than in N, N-dimethylacetamide, so the undissolved indomethacin appeared as a white residue during dialysis. The samples were filtered by a 1 μm syringe filter and were allowed to equilibrate for 24 h and were measured thereafter.

2.4 Characterization

The MALDI-MS measurements were performed with a Bruker BIFLEX III mass spectrometer equipped with a time-of-flight (TOF) mass analyzer. In all cases, a 19 kV acceleration voltage was used with pulsed ion extraction (PIE). The positive ions were detected in the reflectron mode (20 kV). A nitrogen laser (337 nm, 3 ns pulse width, 106-107 W/cm^2) operating at 4 Hz was used to produce laser desorption and 300 shots were summed. The spectra were externally calibrated with a poly(ethylene glycol) standard (Mn = 1450 g/mol, Mw/Mn = 1.02) using linear calibration. Samples were prepared with a DHB matrix (20 mg/mL), an analyte solution of 2 mg/mL, and sodium trifluoroacetate (1 mg/mL) as the cationization agent in methanol. The solutions were mixed in a 10:5:1 (v/v/v) ratio (matrix/analyte/cationiation agent). A volume of 0.5 μL of the solution was deposited onto a metal sample plate and allowed to air-dry. Dynamic Light Scattering (DLS) measurements were carried out on a Brookhaven light scattering instrument equipped with a BI-9000 digital correlator and a temperature-controlled goniometer. The light source was a solid-state vertically polarized laser operating at $\lambda = 533$ nm. Using the methods of cumulants, the effective diameters (d_{eff}) of the micelles were determined from the characteristic decay rate (Γ) of the autocorrelation function of the scattered light at 90°. The particle size distribution was determined at a 90° scattering angle and evaluated by the nonnegative constraint least-squares (NNLS) method.



Sch. 1. The synthesis route to polyisobutylene-*b*-poly(vinyl alcohol)

2.5 Determination of CMC

The count intensity of the scattered light was plotted as a function of the logarithm of the concentration. Two lines were fitted on the initial and final parts of the curve. The CMC was given by the intercept of these lines.

2.6 Size Exclusion Chromatography (SEC)

The M_n and molecular mass distribution (MMD) of the polymers were measured by SEC in THF at 35 °C with a Waters chromatograph equipped with four gel columns (7.8 × 300 mm, 7 μm Ultrastyragel columns: 500, 10^3, 10^4, 10^5 Å), a Waters 600 HPLC pump, and Waters 490E UV and Waters 410 refractive index detectors. The M_n and M_w/M_n values of the oligomers were calculated relative to polyisobutylene.

2.7 NMR Spectroscopy

The ^{1}H spectra were recorded in $CDCl_3$ at 25°C on a BRUKER AM 360 spectrometer with tetramethylsilane as the internal standard.

2.8 UV-Vis Spectroscopy

The UV-Vis spectra were recorded on a HP 8453 diode array spectrometer at 25°C in a glass cuvette of 1 cm optical path length. The absorbance at peak maximum of 321 nm was used for indomethacin concentration calculations.

3 Results and Discussion

A series of PIB-*b*-PVA amphiphilic block copolymers were prepared having the same PIB segment length but a different PVA segment length. The synthesis is outlined in Scheme 1.

First, PIB-*b*-PtBVE block copolymers were prepared. The GPC RI traces (Figure 1) smoothly shifted to lower elution volumes without tailing, indicating ~100% blocking efficiency.

The molecular weights and molecular weight distributions of PIB-*b*-PtBVE samples determined by GPC and ^{1}H-NMR analysis are summarized in Table 1.

The molecular weights determined by different methods are in agreement, although both of these methods become unreliable at higher values. Since the GPC molecular weights are based on a calibration curve obtained with PIB standards, the results are reliable at lower molecular weights (error<10%), however with long P*t*BVE segments the GPC molecular weights are unreliable. The problem of molecular weight determination based on ^{1}H-NMR spectroscopy can be clearly seen in Figure 2.

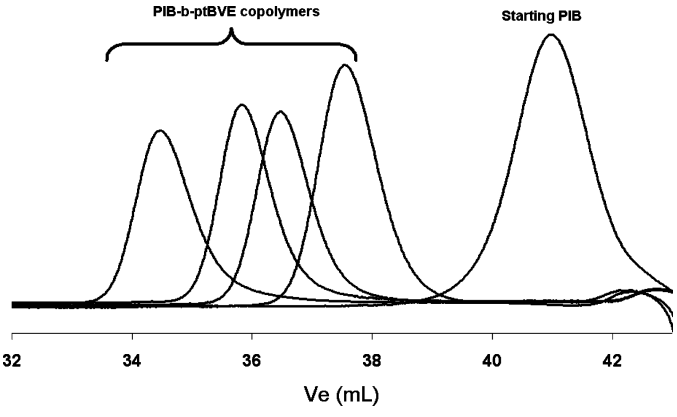


Fig. 1. The GPC RI traces of the starting PIB (right) and that of the PIB-*b*-P*t*BVE copolymers (left). The *t*BVE segment size increases from right to left.

Table 1. The molecular weights and polydispersities of the PIB-*b*-P*t*BVE samples prepared.

Sample Name	M_n *(GPC) (g/mol)*	M_n *(^{1}H-NMR) (g/mol)*	*PDI*
PIB	900	750	1.19
PIB-*b*-P*t*BVE1	5300	5800	1.10
PIB-*b*-P*t*BVE2	11700	13000	1.08
PIB-*b*-P*t*BVE3	17400	18000	1.08
PIB-*b*-P*t*BVE4	25800	24000	1.11

It is mainly due to the overlapping of the main chain signals of the PIB and P*t*BVE segments. Therefore the calculation was based on the signal intensity ratio of the DTE aromatic protons and that of the methylidene (CH) protons of the *t*BVE units. As the M_n increases, so does the intensity of the CH protons, but the relative intensity of the DTE protons decreases and almost fades into the baseline making the M_n calculation difficult. The chain end of the *t*BVE segment was capped with allyltrimethylsilane to avoid the formation of a reactive acetal-type chain end, which can induce the formation of dimers (PIB-*b*-PVA-*b*-PIB) during HBr treatment. As can be seen in the zoomed inset of Figure 1, the allyl protons appear between 4.7-4.8 ppm and based on intensity ratio calculations, the capping efficiency was found to be 100% within experimental error.

The *t*BVE segment was converted into a PVA segment by HBr treatment in dichloromethane. The removal of the *t*Bu groups causes a considerable loss in molecular weights. The resulting PIB-*b*-PVA polymers could be dissolved only in very polar solvents such as water, dimethylformamide, dimethylsulphoxide, and dimethylacetamide. The insolubility in THF hindered the molecular weight determination by GPC. Molecular weight determination by ^{1}H-NMR is also impossible due to the total overlap of the signals of PIB protons and that of the PVA methylene proton as can be seen in Figure 3.

The spectrum is simpler than that of PIB-*b*-PtBVE; it is dominated by two major signals namely the main chain CH protons (at 4 ppm) and CH_2 protons (at 1.6 ppm) of the PVA segment. The absence of the side group methyl proton signals at 1.2 ppm indicates complete conversion of P*t*BVE into PVA. Due to the above problems MALDI-TOF MS measurements were carried out to determine the exact molecular weights of the polymers. A representative spectrum is shown in Figure 4.

The main peak $[M+Na]^+$ belongs to the singly charged copolymer chains; the minor peak $[2M+Na]^+$ consists of two polymer chains and a cation and is characteristic of high molecular weight polymers. The poor resolution of the spectrum is due to the small mass difference of the repeating units and a consecutive water loss of the PVA chains under MALDI conditions. From the spectra, the exact molecular

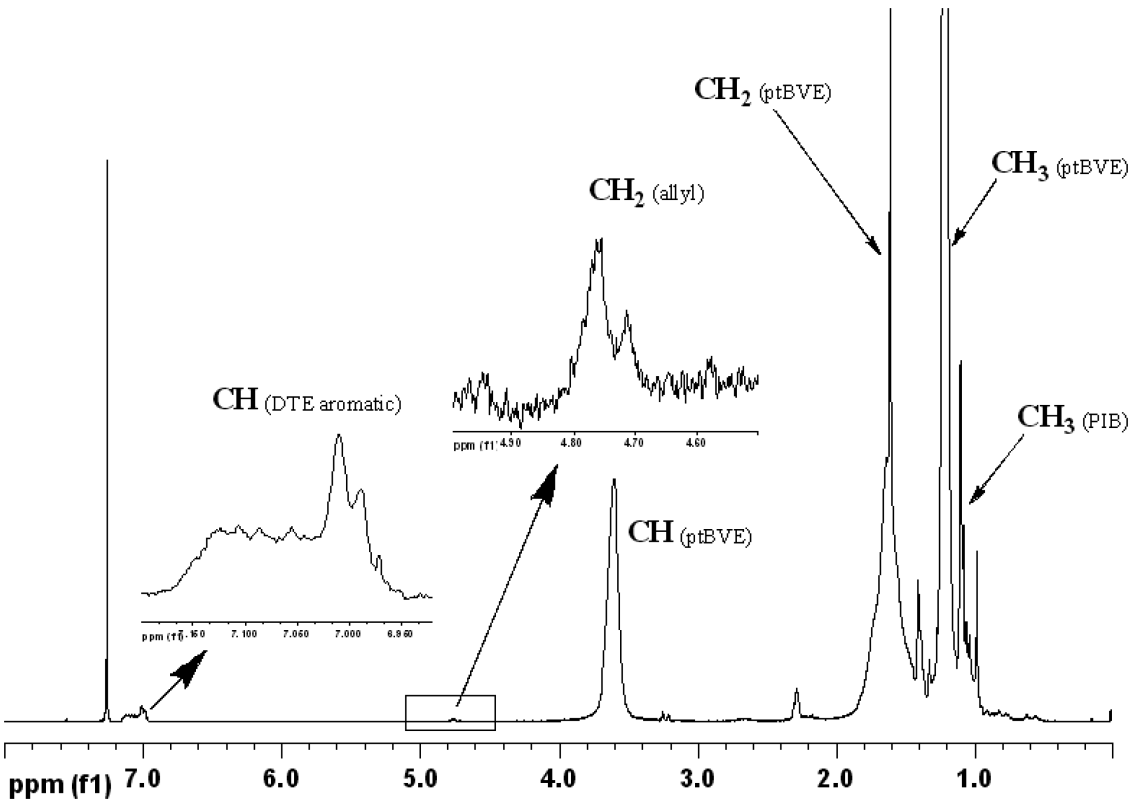


Fig. 2. A representative ^{1}H-NMR spectrum of PIB-*b*-P*t*BVE (solvent: $CDCl_3$, T=298 K, TMS as internal standard).

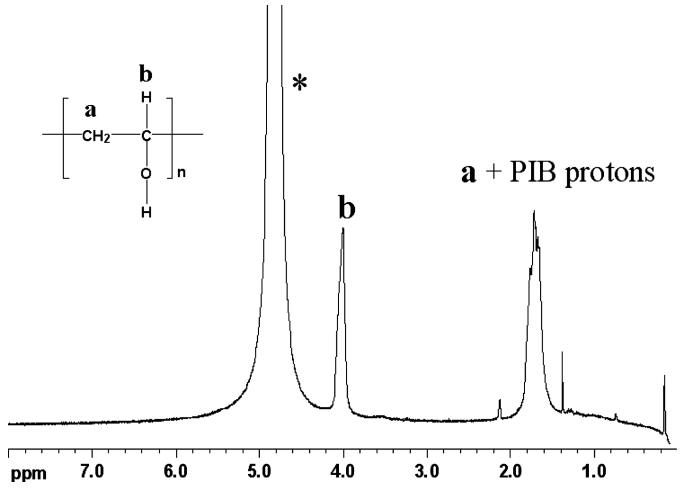


Fig. 3. A representative ^{1}H-NMR spectrum of PIB-*b*-PVA (solvent: D_2O, T=298 K)

weights of the copolymers were determined and, together with the calculated M_ns, are summarized in Table 2.

The calculated and measured M_ns agree well at short PVA segment length, but the difference increases with increasing PVA length. As MALDI TOF MS provides an absolute method for molecular weight determination, the latter values were used.

3.1 Characterization of Micelles. CMC and Micelle Size Determination

Micellar properties were investigated by dynamic light scattering. Since the polymers dissolve in water almost instantly, the first series was prepared by direct dissolution and the second series was prepared by dissolving the samples in N, N-dimethylacetamide. The samples were then

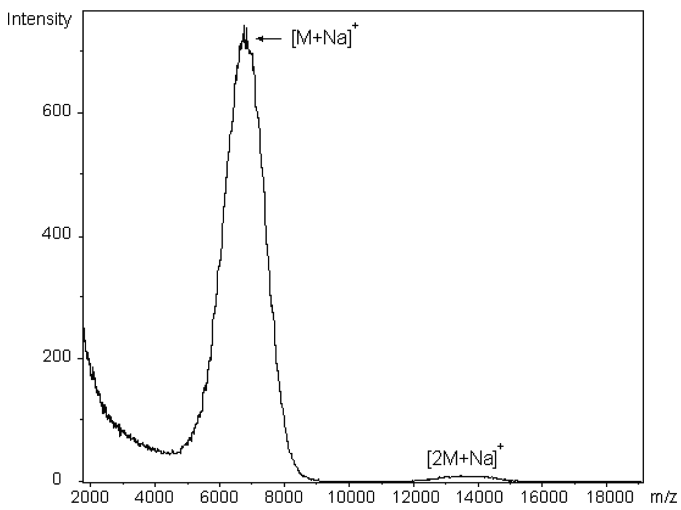


Fig. 4. The MALDI-TOF MS spectrum of PIB-*b*-PVA2 recorded in the linear mode.

Table 2. The molecular weights of the PIB-*b*-PVA samples prepared. (Calculations are based on GPC)

Sample Name	M_n *(calculated) (g/mol)*	M_n *(MALDI) (g/mol)*
PIB-*b*-PVA1	2950	3250
PIB-*b*-PVA2	5800	6500
PIB-*b*-PVA3	8350	9500
PIB-*b*-PVA4	12000	14500

dialyzed in water. Both series were filtered, diluted to get the desired concentration, and equlibrated for 24 h. From dynamic light scattering measurements, the critical micelle concentration and effective micelle size were obtained, which are summarized in Table 3.

It can be seen that the CMC values were lower in the case of direct dissolution than after dialysis. The micelle size, however, was much higher and changed less significantly. A possible explanation can be that PVA chains form strong hydrogen bonds in the solid state, and these aggregates are covered with PIB chains. Therefore water can hardly get to the inside of the solid copolymer and, instead of the complete solution of the single copolymer chains, large aggregates will be present in the aqueous phase. This effect becomes more pronounced with increasing PVA segment length. In the case of PIB-*b*-PVA4 (longest PVA segment), no light scattering could be observed after filtering the opalic solution through a 1 μm membrane filter. Less polar solvents can solvate both segments, which is why the dialysis method is better for solution preparation. In the case of dialyzed aqueous solutions, the CMC values decrease with decreasing PVA segment size in line with our expectations.

3.1.1. *Static Light Scattering Measurements*

For the determination of micellar architecture, SLS measurements were carried out in water at 25°C. The results are summarized in Table 4.

SLS comfirmed that micelle size decreases with increasing molecular weight. At low molecular weight, the size of the apolar (PIB) and polar (PVA) segments are similar. Therefore the formation of core-shell type micelles with high aggregation numbers is likely. The hydrodynamic radii of the micelles differ only slightly from their radii of gyration. The Rg/Rh provides valuable information on micelle shape. Regular values for spherical micelles fall in the range of 0.8–1.3 (26, 27). Our values do not vary significantly (0.78–0.93) with the molecular weight, thus they can assumed to be spherical particles. However, the formation of classical core-shell type micelles is not likely due to the high aggregation numbers, especially for PIB-*b*-PVA1 ($N_{agg} > 10^4$). Therefore the formation of vesicle-like aggregates is the most feasible. As the polar segment size becomes much larger than that of the apolar, the aggregation number decreases dramatically which, together a with strong

Table 3. Micellar parameters of aqueous PIB-*b*-PVA samples determined by DLS.

	Direct dissolution			*Dialysis*		
Copolymers	*cmc (mg/mL)*	*cmc (mmol/mL)*	*Micelle size (nm)*	*cmc (mg/mL)*	*cmc (mmol/mL)*	*Micelle size (nm)*
PIB-*b*-PVA1	0.045	1.38E-5	185	0.056	1.72E-5	180
PIB-*b*-PVA2	0.056	8.61E-6	180	0.071	1.09E-5	130
PIB-*b*-PVA3	0.061	6.42E-6	165	0.100	1.05E-5	105
PIB-*b*-PVA4	—	—	—	0.120	8.27E-6	85

PVA-water interaction, results in smaller micelles. In the case of PIB-*b*-PVA4, $R_g/R_h = 0.78$ is almost equal to the theoretical value (0.775) (27) for hard homogeneous spheres, even though the micelle size and aggregation number are still higher than expected.

3.2 Solubilization of Indomethacin

The aggregates formed in water have an apolar core and can therefore be used as drug delivering nanocontainers. A perfect example of an apolar drug molecule is indomethacin, whose solubilization has been extensively studied recently. Indomethacin is practically insoluble in water, thus the concentration determination of its saturated solution is difficult. A number of different solubility data were reported in the literature (28, 29). We chose UV-Vis spectroscopy for the concentration determination. A stock solution of indomethacin was prepared in ethanol, from which a set of samples was made by dilution with distilled water. The absorbance at the maximum of 321 nm was plotted against concentration and a calibration line was constructed as shown in Figure 5.

As can be seen from Figure 5, the experimental points fit well on a linear starting from the origin. The calibration line above was used in further experiments to obtain the concentration of indomethacin. To investigate the solubilization, copolymer solutions were made in N,N-dimethylacetamide so that the concentration after dialysis would be above their CMCs. Next, indomethacin was added and the mixtures were dialyzed in distilled water for a week. The solutions were filtered and measured by UV-Vis spectroscopy. To eliminate the effect of light scattering and the ensuing increase in absorbance, the dialyzed copolymer solutions were used as blank solutions. The spectra were studied for traces of remaining N,N-dimethylacetamide but its absorption bands were completely missing.

The absorbance was measured at a peak maximum of 321 nm and the concentrations of indomethacin were calculated from the calibration line and are summarized in Table 5.

The concentration of indomethacine increased in every copolymer solution. The effect was the greatest in the case of PIB-*b*-PVA4, as evidenced by a more than tenfold increase in solubility compared to pure water. However, the increase is not linear. To obtain a better comparison, all solubility data were remeasured by applying equal concentrations chosen to be that of the smallest copolymer PIB-*b*-PVA1 (5.76 mg/mL). The new indomethacin concentrations are plotted against copolymer length (polarity) in Figure 6.

As can be clearly seen in Figure 6, a maximum curve was obtained. For a unit concentration (mg/mL), PIB-*b*-PVA2 can solubilize most of the indomethacin. Its solubilization ability is almost doubled compared to those of the other copolymers. This phenomenon can be explained by the micellar properties of the copolymers. Geometrical calculations were thus used to obtain important micellar properties.

For a core-shell type micelle, the radius of the core can be expressed (30,31) as Equation 1:

$$R_c = [3M_{\mathrm{W,mic}} w_{\mathrm{PIB}}/(4\pi N_A \rho_{\mathrm{PIB}} \Phi_{\mathrm{PIB}})]^{1/3} \qquad (1)$$

Table 4. Micellar parameters of PIB-*b*-PVA copolymers obtained by SLS

Copolymers	R_h *(nm)*	R_g/R_h	$M_w \times 10^{-7}$ *(g/mol)*	N_{Agg}
PIB-*b*-PVA1	209	0.86	3.54	10892
PIB-*b*-PVA2	162	0.80	2.30	3538
PIB-*b*-PVA3	113	0.93	1.98	2084
PIB-*b*-PVA4	109	0.78	0.87	600

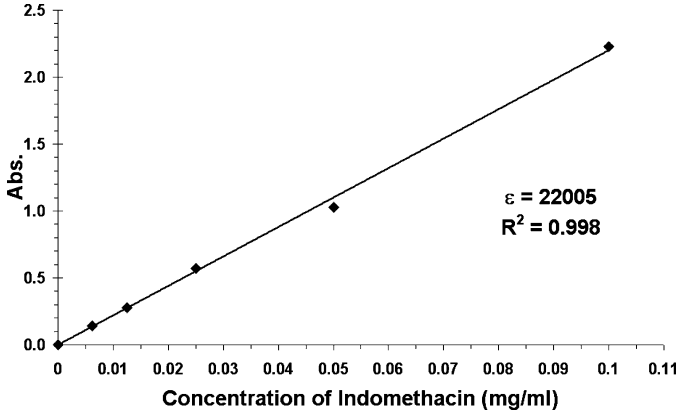


Fig. 5. UV-Vis calibration curve of indomethacin in water (T = 25°C).

Table 5. Solubility data of indomethacine in copolymer solutions in water at 25 °C

	Molecular mass (g/mol)	*Polymer concentartion (mg/mL)*	*Polymer concentartion (mmol/mL)*	*Solubility of indomethacin (mg/mL)*
Water direct solution		0		0.0038
Water		0	0	0.0071
PIB-*b*-PVA1	3250	5.76	0.0018	0.0167
PIB-*b*-PVA2	6500	7.04	0.0011	0.0494
PIB-*b*-PVA3	9500	8.17	0.0009	0.0248
PIB-*b*-PVA4	14500	11.34	0.0008	0.0265

Where $M_{w,mic}$ is the average molecular weight of the micelle, w_{PIB} is the weight fraction of PIB in the copolymer, N_A is Avogadro's number, ρ_{PIB} is the density of PIB (1g/mol), and Φ_{PIB} is the volume fraction of PIB in the core ($\cong$1). The volume of the hydrophobic core (V_c) is given by Equation 2.

$$V_c = \frac{4}{3}\pi R_c \tag{2}$$

The total volume of the hydrophobic cores (V_a) is given by Equation 3.

$$V_a = V_c * ((C - \text{cmc})/N_{\text{agg}}) * N_A \tag{3}$$

where C is the concentration of the copolymer in mol/L, cmc is given in mol/L, N_{agg} is the aggregation number of the micelles.

The incorporation of indomethacin to the micelles can be considered as a simple partitioning equilibrium between the aqueous phase and the micelle core as expressed in Equation 4.

$$[Ind]_a/[Ind]_w = K_v V_a/ V_w \tag{4}$$

The concentration ratios can easily be obtained from the solubility data determined by UV spectroscopy.

Table 6. Geometrical parameters and partition constant data.

Copolymers	w_{PIB}	R_c *(nm)*	V_c *(dm^3)*10^{22}*	V_a *(dm^3)*10^4*	K_v*10^6
PIB-*b*-PVA1	0.231	14.6	131.3	12.7	0.8
PIB-*b*-PVA2	0.115	10.0	42.5	6.3	15.0
PIB-*b*-PVA3	0.079	8.4	25.1	4.3	13.4
PIB-*b*-PVA4	0.051	5.5	7.1	2.8	35.6

The calculated geometrical micellar data are summarized in Table 6.

However, the apolar volume of the aggregates is largest in the case of

PIB-*b*-PVA1. The partition constant is two orders of magnitude less than that of the other copolymers. Only a slight change in K_v was observed for the rest of the copolymers. A possible explanation can be found in the structure of the micelles. At the shortest PVA length, the high aggregation number suggests that we are not dealing with regular core-shell-type micelles, but a vesicle-like structure is most probable. The apolar part of a vesicule is much smaller than that of the same size micelle, therefore fewer indomethacin molecules can be solubilized than in the case of micelles formed from copolymers of a larger PVA segment.

The properties of the doped micelles were also investigated by DLS. Micelle size and CMC values are presented in Figure 7.

The CMC values do not show significant change from that of the pure copolymers; the difference is within the limits of experimental error (<10%). On the other hand the micelle size is reduced significantly. The greatest change can be observed in the case of PIB-*b*-PVA1 (180 nm vs. 102 nm), as the size of the doped micelle is almost half of the original. The size reduction is 40 nm for PIB-*b*-PVA2 and 3, while only 20 nm for PIB-*b*-PVA4.

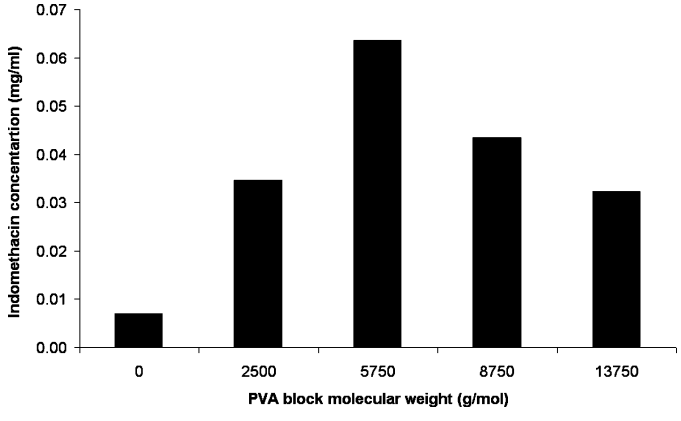


Fig. 6. The concentration of saturated aqueous indomethacin solutions vs. copolymer length. (T=25°C, $C_{copolymer}$ =5.76 mg/mL)

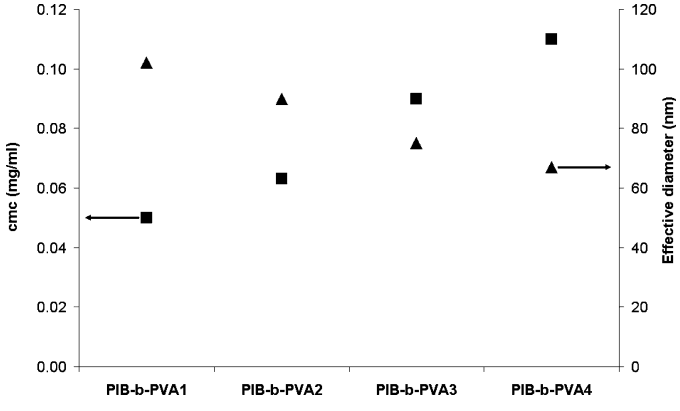


Fig. 7. CMC and micelle size of the doped copolymer aggregates by DLS (water, 25°C, Θ =90°)

4 Conclusions

The synthesis of amphiphilic PIB-*b*-PVA copolymers of varying hydrophilic segment lengths was carried out. The micellization behavior was investigated in aqueous media by dynamic and static light scattering methods. The CMC values are similar to other amphiphilic block copolymers but micelle sizes and aggregation numbers were found to be much higher. The micelles have a more or less spherical shape according to their Rg/Rh ratios, but considering their sizes they cannot be classical core-shell type micelles. Important micellar properties such as the volume of the apolar micelle core were calculated. The hydrophobic cavity of the aggregates was tested as a drug-carrying compartment by doping the aqueous copolymer solutions with indomethacin. The solubility of the water insoluble drug increased in all cases but a large dependence of segment length ratio was found. The best result was obtained in the case of PIB-*b*-PVA2 (1:8 length ratio) where a tenfold increase in indomethacin solubility was observed. From the solubility data a partition constant, K_v, was calculated and was found to be dependent upon the aggregation number. The CMC of the doped copolymers remained unchanged, although the micelle size was reduced significantly.

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